Developing A Predictive Model for Risk of Hospital Readmission After A Colorectal Surgery

A thesis

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Basem Almussallam, MBBS

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Advisors:

Thesis Chair & Program Mentor: Rocco Ricciardi, MD, MPH

Project Mentor: David Kent, MD, CM, MSc

Statistical Mentor: Robin Ruthazer, MPH

ABSTRACT

Identifying patients at high-risk of hospital readmission after colorectal surgery is necessary to help reduce those readmissions. We aimed to develop and internally validate a model that can predict hospital readmission risk for patients undergoing colorectal surgery. Our model was designed to be used before discharging the patient from hospital.

We performed a retrospective cohort analysis on data collected from a colorectal surgery department at a tertiary care center. All patients who underwent colorectal surgery between July 16, 2007 and June 30, 2011 were included. Our main outcome was readmission within 30-days of hospital discharge. Generalized estimating equations were used to measure the association between various clinical and demographic variables and hospital readmission risk, while accounting for the possible correlation between operative encounters caused by patients that had more than one encounter. A backward selection method was used to select variables for the final model. Overall performance, calibration and discrimination of the predictive models were assessed. The model was internally validated using bootstrapping.

In a cohort of 4,522 operative encounters (from 3,628 patients), 449 (9.9%) (from 402 patients) were readmitted to the hospital within 30-days of discharge. The final predictive model included the following factors: age, length of stay, patient setting, comorbidity score, use of alcohol, surgery time, surgery urgency and use of anxiolytic

medications. Longer length of stay (OR=1.02 (1.01, 1.03)), inpatient procedure (OR=3.6 (2.41, 5.38)), higher comorbidity score (OR=1.1 (1.06, 1.17)), not drinking alcohol (OR for drinking=0.6 (0.56, 0.84)), longer surgery time (OR=1.1 (1.07, 1.22)) and anxiolytics use (OR=1.8 (1.40, 2.30)) were all significantly associated with increased readmission risk (p-value <0.05). The model performed similarly in the original and internally validated set. We were limited by the single-center retrospective study nature and we were unable to capture readmissions outside the study center.

In conclusion, the risk of hospital readmission after a colorectal surgery can be predicted using a simple predictive model. Future studies are needed to externally validate this model.

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LIST OF ABBREVIATIONS

AIC:	Akaike information criterion score
ASA:	The American Society of Anesthesiologists score
CI:	Confidence interval
CMS:	The Centers for Medicare and Medicaid Services
c-statistics:	Concordance statistic
GEE:	Generalized estimating equation
OR:	Odds ratio
ROC:	Area under the receiver operator characteristic curve
SD:	Standard deviation
TRIPOD:	Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis statement
VNA:	Visiting Nurse Association

INTRODUCTION

Readmission and Colorectal Surgery:

In the United States alone, more than 600,000 surgical procedures are performed annually for patients with colon diseases. [1] Hospital readmissions, after surgery, are a major concern among those patients. Hospital readmission rates in colorectal surgery population range from 7.3% to 20% in the literature. [2-12] In a study that reviewed commercial health insurance records for patients who underwent colorectal surgery, 30-day readmission rates were found to be 11.4% with a median cost of $ 8,885 per readmission, accounting for approximately $ 300 million nationwide for colorectal surgery alone. [2] Furthermore, hospitals with higher readmission rates are more likely to have higher surgical mortality. [13] The Centers for Medicare and Medicaid Services (CMS) has implemented a readmission reduction program that targeted specific medical diagnoses. [14,15] CMS has recently expanded the diagnosis list[16] and it is likely to cover colorectal diseases in the future.[17]

In order to better address the high readmission rates and associated costs, we need to better understand the important determinants of readmission and better identify those at highest risk. Lucas et al. found that a model that included the American Society of Anesthesiologists (ASA) score and length of stay can predict hospital readmission after general, vascular and thoracic surgeries (c-statistics of 0.696). [18] Lucas's model was not designed to specifically predict hospital readmission after colorectal surgery, which is

likely to have risk factors substantially different from vascular surgery. However, despite the high proportion of readmissions in colorectal surgery, there are no published models that were specifically designed to predict hospital readmission in patients who undergo colorectal surgery.

Colorectal surgeons can better plan patient post-discharge care if they can predict readmission risk after surgery and before hospital discharge. We sought to develop a model that can predict hospital readmission risk for patients who undergo colorectal surgery and internally validate the model.

Readmission and Health Cost:

The United States remains to have the highest health expenditure in the world. According to the 2013 health report of the Organization for Economic Co-operation and Development, the United States health expenditure per capita in 2011 was almost twice or higher than the expenditure of other developing countries. [19] The healthcare cost in the United States is growing every year. National health spending in 2012 is estimated to have reached about three trillion U.S. dollars and to have grown 3.9 percent. [20] Rising concerns among healthcare payers about these high cost has led to efforts to identify areas to reduce spending and improve healthcare services. Hospital readmissions are associated with high costs, decrease in patient satisfaction and substantial load to affected medical establishments. In 2004, an estimated cost of 17 billion U.S. dollars for unplanned hospital readmissions in Medicare patients. [21] A review of the Healthcare Cost and Utilization Project 2011 database, conducted by the Agency for Healthcare Research

and Quality, estimated around 3.3 million readmissions nationwide with a total hospital cost of more than $41 billion. [22] Moreover, some hospital readmissions are potentially preventable[23,24] and have been linked to substandard or inadequate inpatient medical management. [25,26] Thus, hospital readmission rates, for both medical and surgical conditions, have been proposed as a tool to judges the quality of the healthcare service. A nationwide readmission reduction program by the Centers for Medicare and Medicaid Services (CMS) was made to tackle this issue. [14,15] When computing financial reimbursement of the hospitals that serve the government insured patients, the CMS takes into account the readmission rates of these hospitals. Financial penalties are enforced on hospitals with higher than expected readmission rates. The readmission reduction program involves three medical diagnoses, namely, acute myocardial infarction, pneumonia and congestive heart failure. Recently, the program was expanded to include hip/knee arthroplasty and chronic obstructive pulmonary disease. [16] The medical condition list is expected to have an additional expansion to cover more diseases including colorectal diseases.[17]

Post-operative hospital readmissions are becoming a significant concern. Studies showed that hospitals that have high surgical mortality are the ones with high readmission rates and one out of seven patients are readmitted within 30 days of discharge after a major surgical procedure. [13] Recently, surgeons became more interested in exploring different factors that may increase the risk of readmission after surgery. Such interest could help in finding a scientific solution to reduce readmissions. A systemic review of risk prediction models for medical hospital readmission showed that these

models vary in discrimination ability (c-statistic range: 0.55-0.83). [27] The review also found that predictive models with the best performance are the one designed to possibly be used at hospital discharge (c-statistic range: 0.68-0.83). In surgery, Lucas et al. used the National Surgical Quality Improvement Program 2011 data to develop a model that can predict hospital readmission after general, vascular and thoracic surgeries. [18] They found that a simple model that contains ASA score and length of stay during index admission had a c-statistics of 0.696.

Patients of colorectal surgery are among the highest risk populations for readmission. They have procedures that range from benign anorectal to complex pelvic reconstructive surgeries. Colorectal surgeons are often challenge with cases that pose higher risk of hospital readmission. Therefore, a simple tool, that can help to predict patient hospital readmission risk after colorectal surgery, is valuable.

MATERIALS AND METHODS

Patients and Study Design:

Consecutive patients who underwent an inpatient or outpatient colorectal surgery procedure at Lahey Hospital & Medical Center from July 16, 2007 through June 30, 2011 were identified using a prospectively maintained departmental quality assessment tool. Readmission was ascertained in all patients who had one or more colorectal procedures in the operating room. If a patient had more than one procedure, readmission was assessed for each procedure as a separate encounter. We reviewed inpatient and outpatient electronic medical records, which included evidence of readmission to other hospitals. The study was reviewed and approved by the Lahey Hospital & Medical Center Institutional Review Board and a waiver of informed consent was obtained. Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) statement guidelines were followed to guide the reporting of this study (Table 1).[28,29]

Table 1: TRIPOD Checklist (Prediction Model Development and Validation).

Section/Topic	Item		Checklist Item	Page
Title and abstract				
Title	1	D;V	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	Cover page
Abstract	2	D;V	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis,	i, ii

			results, and conclusions.	
Introduction				
Background and objectives	3a	D;V	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	1-4
	3b	D;V	Specify the objectives, including whether the study describes the development or validation of the model or both.	2
Methods				
Source of data	4a	D;V	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	5
	4b	D;V	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	5
Participants	5a	D;V	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	5
	5b	D;V	Describe eligibility criteria for participants.	5
	5c	D;V	Give details of treatments received, if relevant.	NA
Outcome	6a	D;V	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	9
	6b	D;V	Report any actions to blind assessment of the outcome to be predicted.	NA
Predictors	7a	D;V	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	9, 10
	7b	D;V	Report any actions to blind assessment of predictors for the outcome and other predictors.	NA
Sample size	8	D;V	Explain how the study size was arrived at.	10, 11

Missing data	9	D;V	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	10
Statistical analysis methods	10a	D	Describe how predictors were handled in the analyses.	13-18
	10b	D	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	17, 18
	10c	V	For validation, describe how the predictions were calculated.	NA
	10d	D;V	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	18
	10e	V	Describe any model updating (e.g., recalibration) arising from the validation, if done.	NA
Risk groups	11	D;V	Provide details on how risk groups were created, if done.	18
Development vs. validation	12	V	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	NA
Results				
Participants	13a	D;V	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	11, 19-23
	13b	D;V	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	19
	13c	V	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	NA
Model development	14a	D	Specify the number of participants and outcome events in each analysis.	23
	14b	D	If done, report the unadjusted	23-28

			association between each candidate predictor and outcome.	
Model specification	15a	D	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	28
	15b	D	Explain how to the use the prediction model.	29
Model performance	16	D;V	Report performance measures (with CIs) for the prediction model.	30-34
Model-updating	17	V	If done, report the results from any model updating (i.e., model specification, model performance).	NA
Discussion				
Limitations	18	D;V	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	38, 39
Interpretation	19a	V	For validation, discuss the results with reference to performance in the development data, and any other validation data.	36, 39
	19b	D;V	Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.	36-40
Implications	20	D;V	Discuss the potential clinical use of the model and implications for future research.	36-40
Other information				
Supplementary information	21	D;V	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	NA
Funding	22	D;V	Give the source of funding and the role of the funders for the present study.	ii

*Items relevant only to the development of a prediction model are denoted by D, items relating solely to a validation of a prediction model are denoted by V, and items relating to both are denoted D;V. We recommend using the TRIPOD Checklist in conjunction with the TRIPOD Explanation and Elaboration document.

Outcome:

Hospital readmission was our primary outcome of interest, as defined by CMS, as an admission within 30-days of a discharge from the hospital. [15] Outpatients who had same-day surgery were counted as a hospitalization with a length of stay of zero days. Data on discharge date, readmission date and length of stay in initial hospital admission were obtained. The reason for readmission was abstracted manually from electronic medical records by reviewing the readmission diagnosis recorded by the admitting physician. Only the primary diagnosis for readmission was considered. The investigator then classified the reasons based on clinical judgments into the following categories: dehydration, small bowel obstruction/ileus, infection, pain related, bleeding, anastomotic leak/fistula, medical, thromboembolism, stoma related, technical surgical complication and wound-related.

Variables:

Information about preoperative history was retrospectively collected including age, sex, tobacco use, alcohol use, cohabitation (living with someone vs. alone), comorbidity score, use of anxiolytics, and ASA score. Data on patient setting (inpatient vs. outpatient), surgery urgency (urgent vs. elective), involvement of other surgical specialties during surgery (yes vs. no), type of anesthesia (general anesthesia vs. local/conscious sedation), procedure classification (anorectal vs. abdominopelvic), intraoperative complications (≥ 1 complication during surgery e.g. intraoperative bleeding, intraoperative cardiac event, conversion of laparoscopic surgery to open and performance of unplanned procedure), estimated blood loss in milliliters, surgery time in

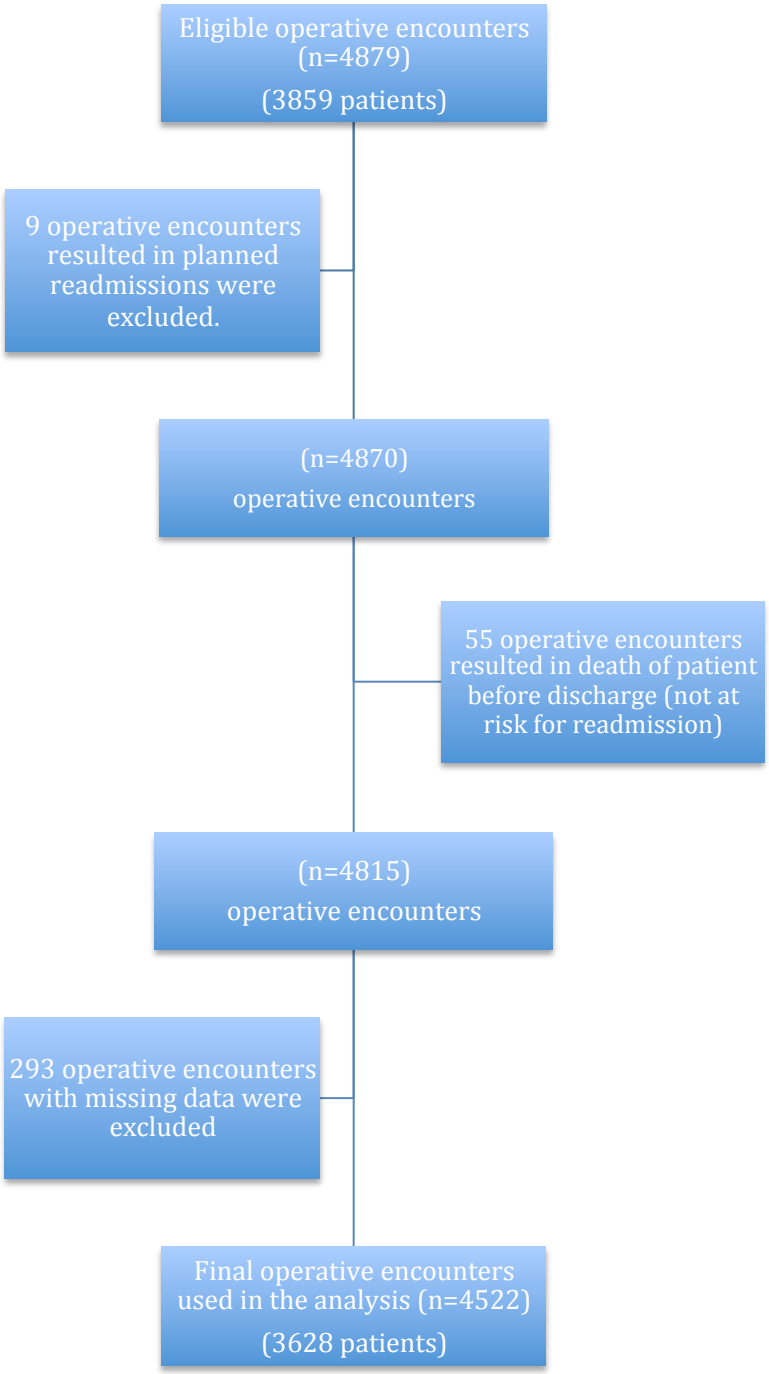
minutes and discharge destination (home without a visiting nurse, home with a visiting nurse or to rehabilitation facility).

Tobacco use was defined as any amount of current preoperative tobacco use. Alcohol use was also defined as any amount of current preoperative alcohol use. Use of anxiolytics was present if both a history of generalized anxiety disorder was established and the patient was currently taking any anxiolytic medications. Non-weighted Charlson Comorbidity Index was used to quantify comorbidity from medical history recorded in medical files. Briefly, the Charlson Comorbidity Index summarizes a patient's comorbid conditions weighted according to mortality risk.[30]

Sample Size and Missing Data:

The final sample size was 4,522 operative encounters (from 3,628 patients) with 449 (9.9%) readmissions (in 402 patients). Figure 1 explains in detail how the final sample size was obtained. Encounters that resulted in planned readmissions or death before discharge were excluded. In addition, we excluded approximately 6% of operative encounters that were missing one or more variables. The variables most frequently missing from operative encounters were surgery time (5% of encounters), estimated blood loss (2% of encounters), intraoperative complication (1% of encounters), cohabitation (0.5% of encounters), alcohol use (< 0.5% of encounters) and tobacco use (< 0.5% of encounters).

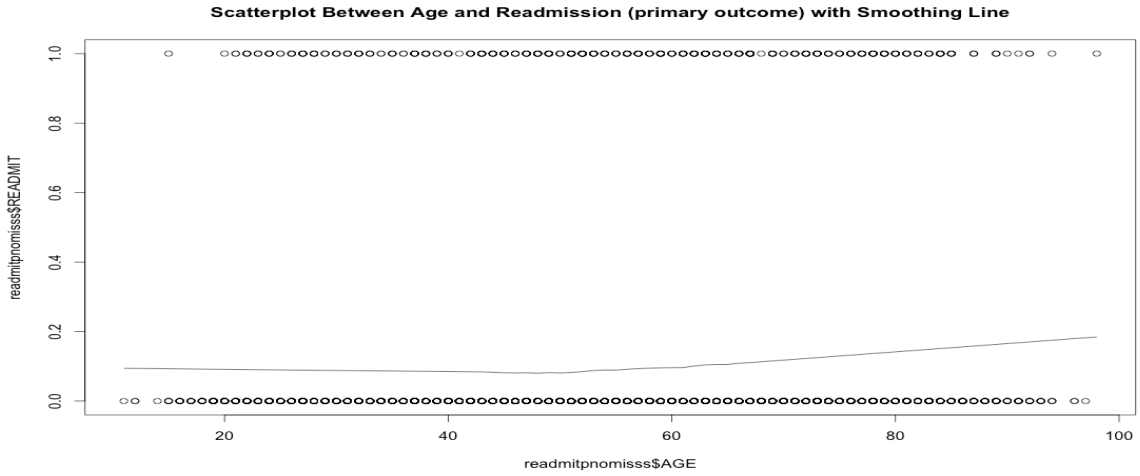
Figure 1: Study flow diagram.



Statistical Analysis:

We used $\chi 2$ tests to compare frequencies across encounters with readmission and encounters without readmission and student's t tests to compare means for continuous data using R statistical package. We examined the linearity of age and length of stay with the dependent variable (Figure 2Figure 3Figure 4Figure 5). We also examined multicolinearity between different variables using correlation tests and variance inflation factor (Table 2Table 3). To account for patients who contributed to more than one operative encounter and the possible subsequent correlation between these encounters, we used generalized estimating equations to measure the association between different variables and readmission risk. A p-value < 0.05 was considered statistically significant.

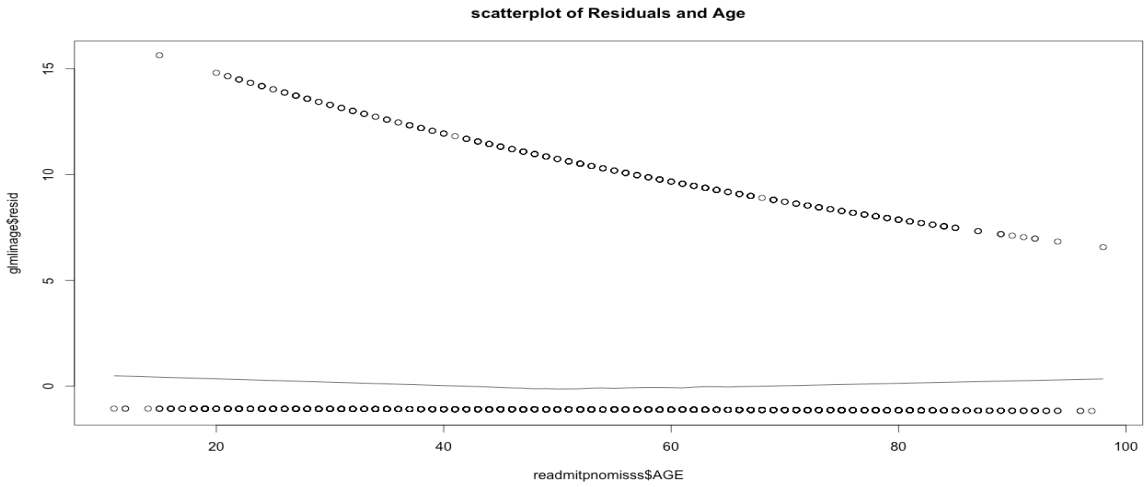
Figure 2: Scatterplot for age in years and readmission with smoothing line.



Interpretation:

- The line is straight then it is slightly increasing around 50 years of age. No obvious quadratic pattern is seen. This could justify the use of age in years without the need for transformation.

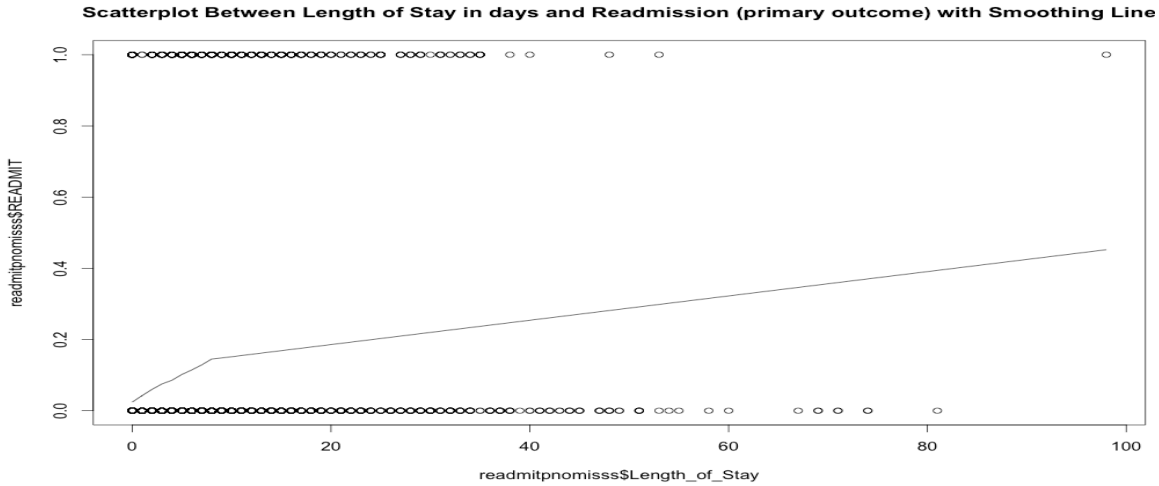
Figure 3: Scatterplot for residuals vs. age in years with smoothing line.



Interpretation:

- The line is almost straight and horizontal around 0. No apparent quadratic pattern. This could justify the use of age in years without the need for transformation.

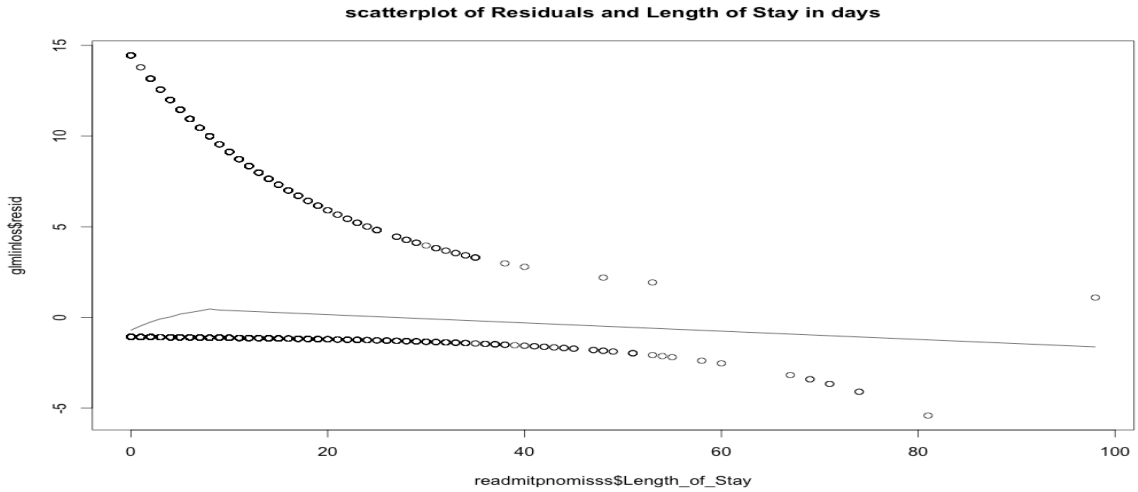
Figure 4: Scatterplot for length of stay in days and readmission with smoothing line.



Interpretation:

- There is a change in the slope of the line approximately at 8 days of length of stay. However, the relation between length of stay and readmission remains in the same direction. The line, grossly, is steadily increasing. No apparent quadratic pattern. This could justify the use of length of stay in days without the need for transformation.

Figure 5: Scatterplot of residuals vs. length of stay in days with smoothing line.



Interpretation:

- Although the line indicates a change in direction of the relation between length of stay and residuals (at approximately 8 days length of stay), the line in general is almost straight and horizontal around 0. No clear quadratic pattern. This could justify the use of length of stay in days without the need for transformation.

Table 2: Pearson's correlation coefficients between variables.

	Age	Gender	Length of stay	Patient setting	Comorbidity score
Age	1.00	0.06	0.23	0.27	0.46
Gender	0.06	1.00	0.05	0.11	0.00
Length of stay	0.23	0.05	1.00	0.48	0.34
Patient setting	0.27	0.11	0.48	1.00	0.27
Comorbidity score	0.46	0.00	0.34	0.27	1.00
Tobacco use	-0.11	-0.01	-0.00	-0.05	-0.00
Alcohol use	-0.10	-0.11	-0.10	-0.11	-0.12

Cohabitation	0.01	-0.06	-0.00	0.02	0.00
Estimated blood loss	0.06	-0.01	0.22	0.18	0.11
Surgery time	0.16	0.04	0.42	0.53	0.15
ASA	0.31	0.01	0.13	0.10	0.23
Intraoperative complications	0.03	0.02	0.04	0.05	0.01
Surgery urgency	-0.00	0.01	0.24	0.22	0.08
Involvement of other surgical specialties during surgery	0.05	0.10	0.12	0.10	0.17
Anxiolytics use	-0.01	0.15	0.10	0.05	0.07

	Tobacco use	Alcohol use	Cohabitation	Estimated blood loss	Surgery time
Age	-0.11	-0.10	0.01	0.06	0.16
Gender	-0.01	-0.11	-0.06	-0.018	0.04
Length of stay	-0.00	-0.10	-0.00	0.22	0.42
Patient setting	-0.05	-0.11	0.02	0.18	0.53
Comorbidity score	-0.00	-0.12	0.00	0.11	0.15
Tobacco use	1.00	0.05	-0.09	-0.01	-0.02
Alcohol use	0.05	1.00	-0.03	-0.00	-0.05
Cohabitation	-0.09	-0.03	1.00	0.01	0.00
Estimated blood loss	-0.01	-0.00	0.01	1.00	0.42
Surgery time	-0.02	-0.05	0.00	0.42	1.00
ASA	0.01	-0.05	-0.03	0.08	0.19
Intraoperative complications	-0.02	-0.01	-0.00	0.20	0.11
Surgery urgency	0.01	-0.03	0.00	0.03	-0.04
Involvement of other surgical specialties during surgery	-0.00	-0.04	0.01	0.02	-0.09
Anxiolytics use	0.11	-0.05	-0.06	0.04	0.05

	ASA	Intraoperative complications	Surgery urgency	Involvement of other surgical specialties during surgery	Anxiolytics use
Age	0.31	0.03	-0.00	0.05	-0.01
Gender	0.01	0.02	0.01	0.10	0.15
Length of stay	0.13	0.04	0.24	0.12	0.10
Patient setting	0.10	0.05	0.22	0.10	0.05
Comorbidity score	0.23	0.01	0.08	0.17	0.07
Tobacco use	0.01	-0.02	0.01	-00	0.11
Alcohol use	-0.05	-0.01	-0.03	-0.04	-0.05
Cohabitation	-0.03	-0.00	0.00	0.01	-0.06
Estimated blood loss	0.08	0.20	0.03	0.02	0.04
Surgery time	0.19	0.11	-0.04	-0.09	0.05
ASA	1.00	0.02	-0.17	0.01	0.03
Intraoperative complications	0.02	1.00	-0.01	-0.00	-0.02
Surgery urgency	-0.17	-0.01	1.00	0.06	0.01
Involvement of other surgical specialties during surgery	0.01	-00	0.06	1.00	-0.01
Anxiolytics use	0.03	-0.02	0.01	0.07	1.00

Interpetation:

- No great concern about colinearity. Majority of correlations coefficients are < 0.3 and non are >0.6.

Table 3: Variance inflation factor (vif) for variables.

	vif
Age	1.45
Gender	1.07
Length of stay	1.73
Patient setting	1.83
Comorbidity score	1.46
Tobacco use	1.05
Alcohol use	1.04
Cohabitation	1.03
Estimated blood loss	1.31
Surgery time	1.94
ASA	1.22
Intraoperative complications	1.04
Surgery urgency	1.20
Involvement of other surgical specialties during surgery	1.10
Anxiolytics use	1.07

Interpetation:

- All vifs are < 2 which may indicates less concern about colinearity.

Model Development:

The final predictive model was developed in two steps. First, a priori variables were selected based on clinical importance using clinical judgments and scientific literature review. These candidate variables included age, sex, length of stay, patient setting, comorbidity score, tobacco use, alcohol use, cohabitation, estimated blood loss, surgery time, ASA score, intraoperative complication, surgery urgency, involvement of other surgical specialty during surgery, anxiolytics use and procedure class. Then, we used backward selection and traditional logistic regression, comparing Akaike information criterion (AIC) scores, to obtain the final model (i.e. retaining the variables that yeilded the lowest AIC score). These selected variables were then used in a

generalized estimating equation (GEE) model to get the final parameter estimates and confidence intervals accounting for the multiple admissions for some patients.

Model performance and validation:

Model performance was assessed using different measures. Model discrimination was evaluated using area under the receiver operator characteristic (ROC) curves. Calibration plots and Hosmer-Lemeshow methods were used to assess model calibration. Risk groups were created by dividing the data to ten groups equal in size sorted by predicted risk from the model. A pseudo R square statistic and the Brier score were used to assess model fitness. The model was internally validated using bootstrapping method.

Subset analysis on pre-specified risk groups:

To justify development of a model for the entire colorectal surgery population, subset analyses were performed comparing univariate associations of risk factors with the outcome between clinically important subgroups (inpatient vs. outpatient, anorectal vs. abdominopelvic procedures and elective vs. urgent surgeries). We also tested the final predictive model performance on these subgroups without re-estimation or re-calibration.

RESULTS

Demographics:

Results are presented from the total of 4,522 operative encounters from 3,628 patients. See Table 4Table 5Table 6Table 7 for details on breakdown of operative encounters by patients. Unless noted otherwise, data are described for the cohort using encounter as the unit of analysis. The median age of the cohort was 54.8 years (SD=16.8, range 11 – 98 years). Almost half of the study participants were women. Alcohol was used by a little bit more than half of the cohort and a majority lived with someone at home. Two thirds had their procedure performed as an inpatient and almost all were done under general anesthesia (Table 8). The most common procedures performed were examination under anesthesia 16%, anal fistula surgery 11%, right colectomy 11% and left colectomy 9%. See Table 9 for further details on types of procedure performed during the study period and associated readmission rates.

Table 4: Breakdown of all operative encounters by number of patients for final dataset used in analysis.

Group	Appeared in Data	Number of Patients	Operative Encounter
1	12	1	12
2	8	3	24
3	7	3	21
4	6	7	42
5	5	7	35
6	4	32	128
7	3	106	318
8	2	473	946
9	1	2996	2996
Total	-	3628	4522

Table 5: Breakdown of operative encounters that resulted in readmission by number of patients for final dataset used in analysis.

Group	Appeared in Data	Number of Patients	Operative Encounter
1	4	4	16
2	3	3	9
3	2	29	58
4	1	366	366
Total	**-**	**402**	**449**

Table 6: Breakdown of all operative encounters that resulted in readmission by number of patients for initial dataset.

Group	Appeared in Data	Number of Patients	Operative Encounter
1	12	1	12
2	9	1	9
3	8	2	16
4	7	3	21
5	6	9	54
6	5	9	45
7	4	43	172
8	3	117	351
9	2	525	1050
10	1	3149	3149
Total	**-**	**3859**	**4879**

Table 7: Breakdown of operative encounters that resulted in readmission by number of patients for initial dataset.

Group	Appeared in Data	Number of Patients	Operative Encounter
1	4	4	16
2	3	3	9
3	2	36	72
4	1	395	395
Total	**-**	**438**	**492**

Table 8: Baseline characteristics of operative encounters for all patients, patients who were not readmitted and patients who were readmitted within 30 days of discharge.

Variable	All (n=4522)	Not readmitted (n=4073)	Readmitted (n=449)	p-value
Age in years Mean (SD)	54.8 (16.8)	54.5 (16.7)	57.7 (17.6)	0.0006
Female n (%)	2199 (48.6)	1954 (48.0)	245 (54.6)	0.012
Length of stay in days Mean (SD)	6.3 (8.4)	5.8 (8.1)	10.9 (9.6)	<0.0001
Inpatient n (%)	3119 (69.0)	2702 (66.3)	417 (92.9)	<0.0001
Charlson Comorbidity Score Mean (SD)	1.6 (2.1)	1.5 (1.9)	2.4 (2.5)	<0.0001
Tobacco use n (%)	696 (15.4)	632 (15.5)	64 (14.3)	0.49
Alcohol use n (%)	2776 (61.4)	2556 (62.8)	220 (49.0)	<0.0001
Lives with someone n (%)	3604 (79.7)	3250 (79.8)	354 (78.8)	0.64
Estimated Blood loss in ml Mean (SD)	90.5 (279.4)	81.7 (236.6)	170.5 (521.3)	0.007
Surgery time in minutes Mean (SD)	102.9 (92.3)	98.1 (89.0)	146.5 (108.5)	<0.0001
ASA* Score Mean (SD)	2.9 (0.8)	2.9 (0.8)	3.1 (0.9)	0.0003
Intraoperative complications n (%)	27 (0.6)	21 (0.5)	6 (1.3)	0.039
Urgent surgeries n (%)	1079 (23.9)	933 (22.9)	146 (32.5)	<0.0001
Involvement of other surgical specialty during surgery n (%)	204 (4.5)	177 (4.4)	27 (6.0)	0.11
Use of Anxiolytics n (%)	935 (20.7)	782 (19.2)	153 (34.1)	<0.0001
Abdominopelvic procedure n (%)	2367 (52.3)	2053 (50.4)	314 (69.9)	<0.0001
General Anesthesia n (%)	4130 (91.3)	3688 (90.6)	442 (98.4)	<0.0001
Discharge Destination n (%) Home without VNA** service Home with VNA** service Rehabilitation facility	 3345 (74.0) 804 (17.8) 373 (8.2)	 3124 (76.7) 664 (16.3) 285 (7.0)	 221 (49.2) 140 (31.2) 88 (19.6)	<0.0001

*ASA: American Society of Anesthesiologists score.

**VNA: Visiting Nurse Association.

Table 9: Extended procedure classification (25 classes) with readmission rates for each procedure class.

Surgery type	Not readmitted	Readmitted	% Readmitted
Total proctocolectomies	30	13	30.23
Stoma creation	163	43	20.87
Pouch related	42	11	20.75
Subtotal colectomies	116	26	18.31
Small bowel obstruction	201	43	17.62
Proctoectomies	237	46	16.25
Continence	16	3	15.79
Other abdominal surgeries	19	3	13.64
Left colectomies	372	52	12.26
Takedown Ileum	197	26	11.66
Takedown Colectomies	73	9	10.98
Right colectomies	457	54	10.57
Rectal prolapse	79	9	10.23
Exploration laparotomies	56	6	9.68
Hernia repair	75	8	9.64
Anal fissure	19	2	9.52
Transanal excisions	111	10	8.26
Sacrum	12	1	7.69
Appendectomies	240	19	7.34
Anal sphincter	16	1	5.88
Advancement flap repair	33	2	5.71
Examination under	697	33	4.52
Hemorrhoidectomies	243	11	4.33
Anal fistula	473	18	3.67
Pilonidal sinus	96	0	0.00
Total	**4073**	**449**	100.00

Readmission:

449 (9.9%) out of 4,522 operative encounters resulted in a readmission within 30-days of discharge after colorectal surgery. Table 8 shows the baseline characteristics of the operative encounters by 30-days readmission status. Patients in the readmitted group were more likely to be older, female and to have undergone an inpatient procedure. They also had a longer average length of stay during initial admission, more comorbidities, more blood loss during surgery and longer surgery time. The most frequent reasons for

readmission were infection related (23%), bowel obstruction or ileus (20%), dehydration (12%), medical (11%), pain control (8%) and bleeding (7%).

Model development:

Using model development steps, described in the method section, on 4,522 encounters with no missing data, the following variables remained in the final model: age, length of stay, patient setting, comorbidity score, alcohol use, surgery time, surgery urgency and anxiolytics use. The final model yielded an AIC score of 2660 compared to the model with all priori selected variables that yielded an AIC score of 2671.

Table 10 shows the unadjusted and adjusted odds ratios of variables in the final model. After adjustment, risk of readmission (p-value < 0.05) was positively associated (at a p-value < 0.05) with: length of stay in days (OR=1.02 (1.01, 1.03)); inpatient procedures (OR=3.6 (2.41, 5.38)); comorbidity score (OR=1.1 (1.06, 1.17)); surgery time in hours (OR=1.1 (1.07, 1.2)); and anxiolytics use (OR=1.9 (1.47, 2.32)); and was negatively associated (at a p-value < 0.05) with alcohol drinking (OR=0.7 (0.56, 0.84)). The effects of age and surgery urgency, although not statistically significant, were retained in the model based on AIC criteria. With some exceptions, the estimates of effects in subset univariate analysis of prespecified subgroups were in the same direction (Table 11Table 12 andTable 13), which justifies the development of a model for the entire colorectal surgery population.

Table 10: Unadjusted and adjusted odds ratios (OR) with 95% confidence intervals for variables in the final model (n=4522 operative encounters).

Variable	Unadjusted OR (95% C.I.)	Adjusted OR (95% C.I.)	P-value
Age in decade (10 years)	1.12 (1.05, 1.2)	0.95 (0.88, 1.02)	0.18
Length of stay in days	1.05 (1.04, 1.06)	1.02 (1.01, 1.03)	0.001
Inpatient (ref=Outpatient)	6.61 (4.58, 9.54)	3.60 (2.41, 5.38)	<0.0001
Comorbidity Score	1.20 (1.15, 1.24)	1.11 (1.06, 1.17)	<0.0001
Alcohol (ref=Not Drinker)	0.57 (0.47, 0.70)	0.68 (0.56, 0.84)	0.0004
Surgery time in hours	1.31 (1.25, 1.39)	1.14 (1.07, 1.22)	0.0001
Surgery Urgency (ref=Elective)	1.62 (1.31, 2.01)	1.19 (0.94, 1.51)	0.14
Anxiolytics (ref=Not User)	2.18 (1.75, 2.71)	1.85 (1.47, 2.32)	< 0.0001

Table 11: Univariate analysis by patient setting.

Variable	Estimate	S. E.	OR (95% C.I.)	p-value
Age in years	0.0034	0.0035	1.0034 (0.9965, 1.0103)	0.33
	-0.0151	0.0131	0.99 (0.96, 1.01)	0.25
Gender (ref = Male)	0.0883	0.1103	1.09 (0.88, 1.36)	0.42
	0.5685	0.3596	1.77 (0.87, 3.57)	0.11
Length of stay in days	0.0317	0.0049	1.03 (1.02, 1.04)	<0.0001
	-	-	-	-
Charlson Comorbidity Score	0.1142	0.0229	1.12 (1.07, 1.17)	<0.0001
	0.2304	0.0802	1.26 (1.08, 1.47)	0.004
Tobacco use (ref = Non user)	-0.0129	0.1543	0.99 (0.73, 1.34)	0.93
	0.0244	0.4599	1.03 (0.42, 2.52)	0.95
Alcohol user (ref = Non user)	-0.4560	0.1099	0.63 (0.51, 0.79)	<0.0001
	-0.3202	0.3708	0.73 (0.35, 1.5)	0.38
Cohabitation (ref = Lives alone)	-0.1274	0.1316	0.88 (0.68, 1.14)	0.33
	0.2023	0.4581	1.22 (0.50, 3)	0.65
Estimated Blood Loss in ml	0.0004	0.0002	1.0004 (1.0001, 1.0007)	0.013
	0.0148	0.005	1.02 (1, 1.03)	0.003
Surgery time in minutes	0.0023	0.0005	1.0023 (1.0013, 1.0034)	<0.0001
	0.0125	0.0058	1.01 (1, 1.02)	0.03
ASA* Score	0.1429	0.0664	1.15 (1.01, 1.3)	0.03
	0.656	0.3039	1.93 (1.06, 3.50)	0.03
Intraoperative complications (ref = No complication)	0.6226	0.4661	1.86 (0.75, 4.65)	0.18
	-	-	-	-
Surgery urgency (ref =	-0.2441	0.1131	0.78 (0.63, 0.98)	0.03

Urgent)				
	1.236	1.0202	3.44 (0.47, 25.4)	0.22
Involvement of other surgical specialty during surgery (ref = No involvement)	0.0417	0.2190	1.04 (0.68, 1.6)	0.85
	1.0703	1.0488	2.92 (0.37, 22.78)	0.308
Use of anxiolytics (ref = Non user)	0.7572	0.1175	2.13 (1.69, 2.69)	<0.0001
	0.2925	0.4345	1.34 (0.57, 3.14)	0.5
Procedure class (ref = Abdmoinopelvic)	0.0077	0.1238	1.0077 (0.791, 1.285)	0.95
	-0.7294	1.0396	0.48 (0.06, 3.70)	0.48
Anesthesia type (ref = Local/conscious sedation)	2.018	1.012	7.52 (1.04, 54.72)	0.046
	0.3423	0.4576	1.41 (0.57, 3.45)	0.455
Discharge Destination (ref = Home without VNA** service)	-	-	-	-
Home with VNA** service	0.6439	0.1236	1.9 (1.49, 2.43)	<0.0001
	-	-	-	-
Rehabilitation facility	1.0238	0.1527	2.78 (2.1, 3.76)	<0.0001
	-	-	-	-

Inpatient is highlighted in light blue vs. Outpatient is highlighted in white.

Comment: Most of the estimates of effect go in the same direction except for age, tobacco use, cohabitation, surgery urgency and procedure class. However, the p-values for age, tobacco use, cohabitation, and surgery urgency are not statistically significant for both subgroups and for procedure class not statistically significant for outpatient subgroup.

Table 12: Univariate analysis by procedure class.

Variable	Estimate	S. E.	OR (95% C.I.)	p-value
Age in years	0.0199	0.0066	1.02 (1.01, 1.03)	0.0023
	0.0031	0.0040	1.0031 (0.995, 1.0120)	0.442
Gender (ref = Male)	0.4081	0.1868	1.5 (1.04, 2.17)	0.029
	0.1127	0.126	1.12 (0.87, 1.43)	0.371

Length of stay in days	0.082	0.0153	1.09 (1.05, 1.12)	<0.0001
	0.0327	0.0055	1.03 (1.02, 1.04)	<0.0001
Patient setting (ref = Outpatient)	1.911	0.2095	6.76 (4.48, 10.2)	<0.0001
	1.174	1.0254	3.23 (0.43, 24.14)	0.252
Charlson Comorbidity Score	0.2855	0.0344	1.33 (1.24, 1.42)	<0.0001
	0.0967	0.0265	1.1 (1.05, 1.16)	0.0003
Tobacco use (ref = Non user)	0.0181	0.2545	1.02 (0.62, 1.68)	0.94
	-0.103	0.1791	0.9 (0.64, 1.28)	0.57
Alcohol user (ref = Non user)	-0.824	0.1846	0.44 (0.31, 0.63)	<0.0001
	-0.3769	0.1257	0.69 (0.54, 0.88)	0.003
Cohabitation (ref = Lives alone)	-0.0170	0.2291	0.98 (0.63, 1.5)	0.94
	-0.1391	0.1514	0.87 (0.65, 1.17)	0.36
Estimated Blood Loss in ml	0.0007	0.0006	1.0007 (0.9995, 1.0020)	0.241
	0.0006	0.0002	1.0006 (1.0002, 1.001)	0.005
Surgery time in minutes	0.0056	0.0008	1.0056 (1.0041, 1.0071)	<0.0001
	0.0027	0.0007	1.0027 (1.0014, 1.004)	<0.0001
ASA* Score	0.6167	0.157	1.85 (1.36, 2.5)	<0.0001
	0.1173	0.0757	1.13 (0.97, 1.3)	0.12
Intraoperative complications (ref = No complication)	2.0319	0.7134	7.63 (1.89, 30.88)	0.004
	0.2705	0.6354	1.31 (0.38, 4.55)	0.67
Surgery urgency (ref = Urgent)	-0.4489	0.2328	0.64 (0.41, 1.01)	0.054
	-0.2643	0.1265	0.77 (0.60, 0.98)	0.037
Involvement of other surgical specialty during surgery (ref = No involvement)	0.4532	0.4393	1.57 (0.67, 3.72)	0.3
	0.1526	0.2458	1.17 (0.72, 1.89)	0.54
Use of anxiolytics (ref = Non user)	0.607	0.2073	1.84 (1.22, 2.8)	0.003
	0.8275	0.1334	2.29 (1.76, 2.97)	<0.0001
Anesthesia type (ref = Local/conscious sedation)	1.4412	0.3925	4.23 (1.96, 9.12)	0.0002
	-	-	-	-
Discharge Destination (ref = Home without VNA** Service)	-	-	-	-
Home with VNA** Service	1.3479	0.2240	3.85 (2.5, 5.97)	<0.0001
	0.7454	0.1424	2.11 (1.59, 2.79)	<0.0001

Rehabilitation facility	1.7994	0.2889	6.05 (3.43, 10.65)	<0.0001
	1.0999	0.1723	3 (2.14, 4.21)	<0.0001

Anorectal is highlighted in light blue vs. Abdominopelvic is highlighted in white

Comment: All estimates of effect go in the same direction except for tobacco use that has not statistically significant p-value for both subgroups.

Table 13: Univariate analysis by surgery urgency.

Variable	Estimate	S. E.	OR (95% C.I.)	p-value
Age in years	0.0113	0.0041	1.01 (1, 1.02)	0.006
	0.0121	0.0056	1.01 (1, 1.02)	0.032
Gender (ref = Male)	0.3086	0.1234	1.36 (1.07, 1.73)	0.012
	0.1436	0.1856	1.16 (0.8, 1.66)	0.439
Length of stay in days	0.0682	0.0082	1.07 (1.05, 1.09)	<0.0001
	0.0304	0.006	1.03 (1.02, 1.04)	<0.0001
Patient setting (ref = Outpatient)	1.7371	0.1933	5.68 (3.89, 8.30)	<0.0001
	3.217	1.0082	24.96 (3.46, 180.03)	0.001
Charlson Comorbidity Score	0.1639	0.0257	1.18 (1.12, 1.24)	<0.0001
	0.1775	0.0317	1.19 (1.12, 1.27)	<0.0001
Tobacco use (ref = Non user)	-0.1351	0.1758	0.87 (0.62, 1.23)	0.44
	-0.0634	0.2436	0.94 (0.58, 1.51)	0.80
Alcohol user (ref = Non user)	-0.5236	0.1229	0.59 (0.47, 0.75)	<0.0001
	-0.5987	0.1867	0.55 (0.38, 0.79)	0.001
Cohabitation (ref = Lives alone)	0.0401	0.1517	1.04 (0.77, 1.4)	0.79
	-0.2701	0.2141	0.76 (0.5, 1.16)	0.2
Estimated Blood Loss in ml	0.0007	0.0004	1.0007 (1.00004, 1.0014)	0.0375
	0.0009	0.0004	1.0009 (1.0001, 1.0016)	0.0185
Surgery time in minutes	0.005	0.0005	1.0051 (1.004, 1.0061)	<0.0001
	0.0041	0.001	1.0041 (1.0021, 1.0061)	<0.0001
ASA* Score	0.5168	0.1079	1.68 (1.4, 2.07)	<0.0001
	0.1227	0.0842	1.13 (0.96, 1.33)	0.145
Intraoperative complications (ref = No complication)	0.8417	0.5562	2.32 (0.78, 6.9)	0.13
	1.4599	0.9173	4.31 (0.71, 25.99)	0.11
Involvement of other surgical specialty during	0.2424	0.2900	1.27 (0.72, 2.25)	0.403

surgery (ref = No involvement)				
	0.3171	0.3211	1.37 (0.73, 2.58)	0.32
Use of anxiolytics (ref = Non user)	0.8854	0.1304	2.42 (1.88, 3.13)	<0.0001
	0.5031	0.2057	1.65 (1.11, 2.48)	0.0145
Procedure class (ref = Abdominopelvic)	-0.8109	0.1266	0.45 (0.35, 0.57)	<0.0001
	-0.6263	0.2349	0.54 (0.34, 0.85)	0.008
Anesthesia type (ref = Local/conscious sedation)	1.6298	0.3860	5.1 (2.40, 10.87)	<0.0001
	-	-	-	-
Discharge Destination (ref = Home without VNA** Service)	-	-	-	-
Home with VNA** Service	1.1066	0.1392	3.02 (2.3, 3.97)	<0.0001
	0.8913	0.2196	2.44 (1.59, 3.75)	<0.0001
Rehabilitation facility	1.4947	0.189	4.46 (3.1, 6.46)	<0.0001
	1.1926	0.2394	3.3 (2.06, 5.27)	<0.0001

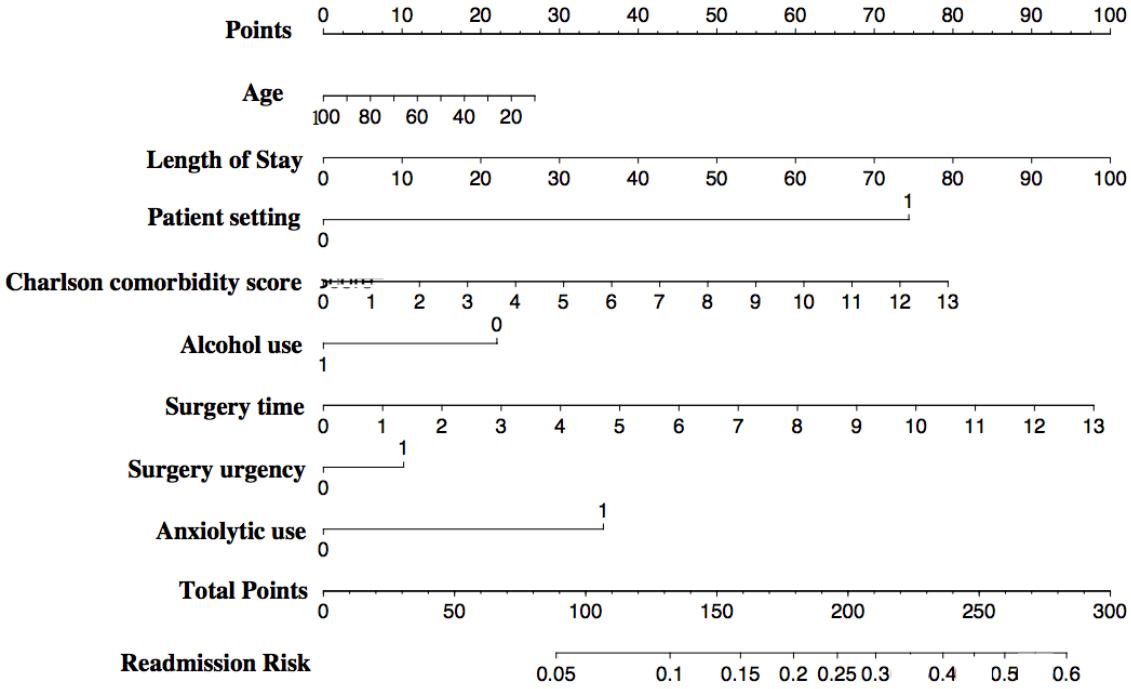
Elective is highlighted in light blue vs. Urgent is highlighted in white

Comment: All estimates of effect go in the same direction except for cohabitation that has not statistically significant p-value for both subgroups.

Model specification:

The exact beta coefficients for the model are: intercept (-3.4), age in years (-0.01), length of stay in days (0.02), patient setting (1.28), comorbidity score (0.11), alcohol use (-0.38), surgery time in hours (0.13), surgery urgency (0.18) and anxiolytics use (0.61). Figure 6 is a graphical representation of the final model in a nomogram.

Figure 6: A nomogram of the final predictive model (n=4522 operative encounters).



Age in years, Length of stay in days, Patient setting (inpatient = 1, outpatient =0), Alcohol use (drink =1, don't drink =0), Surgery time in hours, surgery urgency (urgent = 1, elective = 0), Anxiolytic use (user = 1, not a user = 0).

To illustrate the model, we considered a hypothetical two patients, first patient of age 56 years undergoing an elective colorectal surgery lasting for one hour and a 5-day inpatient stay. This patient has a comorbidity score of 1, drinks alcohol and doesn't use anxiolytics, and thus has a low probability of 6.2% to be readmitted to hospital. The second hypothetical patient is 50 years old who had an urgent inpatient colorectal surgery lasting for three hours and stayed in hospital for 10 days. This patient has a comorbidity score of 4, drinks alcohol and use anxiolytics medications, and thus has a high probability of 23.5% to be readmitted to hospital.

Model performance:

In regard to model discrimination, our model showed a c-statistic of 0.732 (95% CI 0.709 – 0.755). Figure 7 presents the ROC curve for hospital readmission after colorectal surgery. Figure 8 displays the calibration plot of our readmission model. In the calibration plot, the risk groups were divided into ten equal risk groups for comparison. Within each risk group, the predicted and observed probabilities were similar indicating a well-calibrated model. So, within our study sample the model performs well within each risk group. The decile with highest risk group showed a predicted readmission risk of 26.6% with a true readmission rate of 25.2%. In contrast, the decile with the lowest risk group showed a predicted readmission risk of 1.6% with a true readmission rate of 1.8%. Our model yielded a pseudo R square statistic of 0.128 and Brier score of 0.084. We also tested the final predictive model performance on the prespecified subgroups (Figure 9Figure 10Figure 11Figure 12Figure 13Figure 14).

Figure 7: ROC curve for risk of hospital readmission after a colorectal surgery (n=4522 operative encounters).

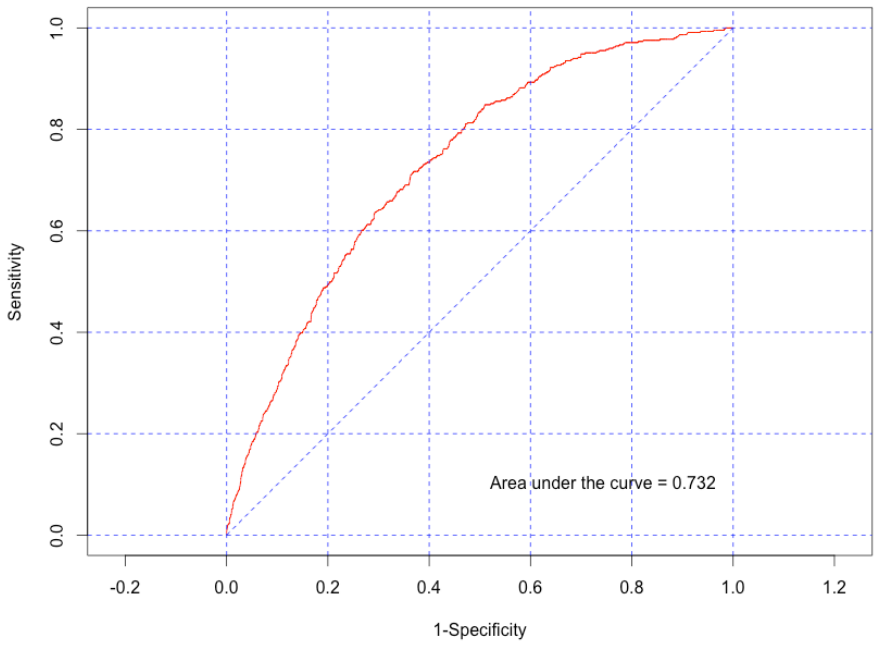
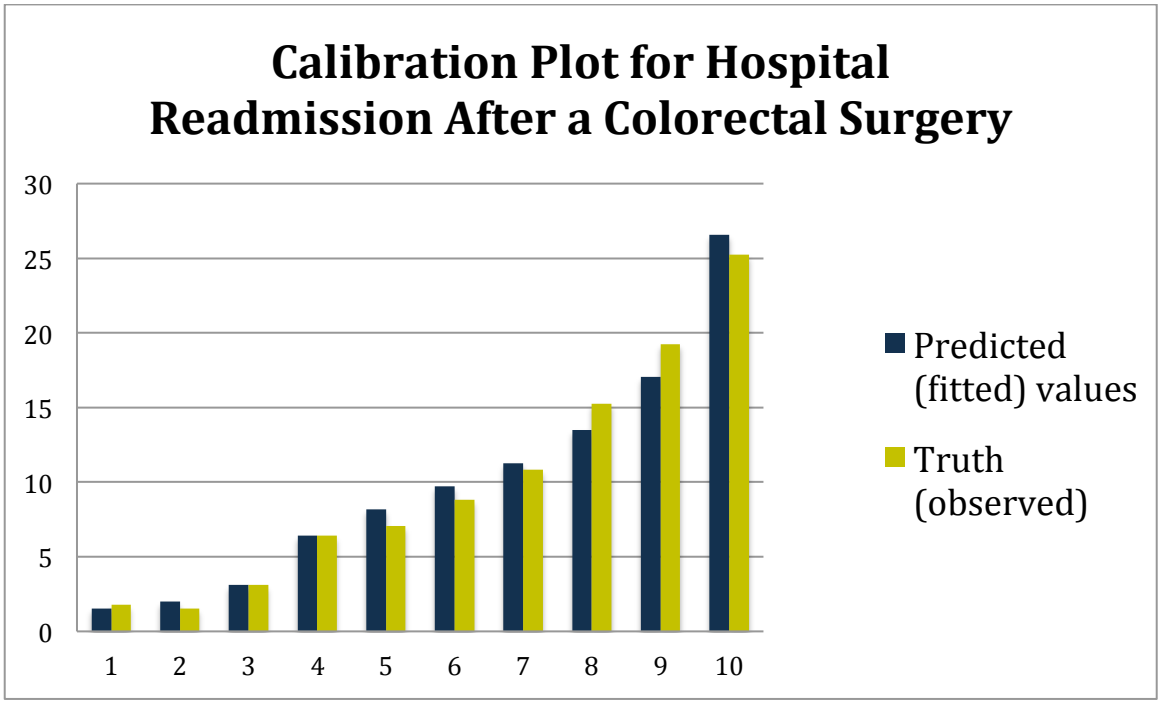


Figure 8: Calibration plot for hospital readmission after a colorectal surgery divided into equal risk groups (n=4522 operative encounters).



x-axis: Decile risk group and y-axis: Precent readmitted

Figure 9: Model performance plot for inpatient group.

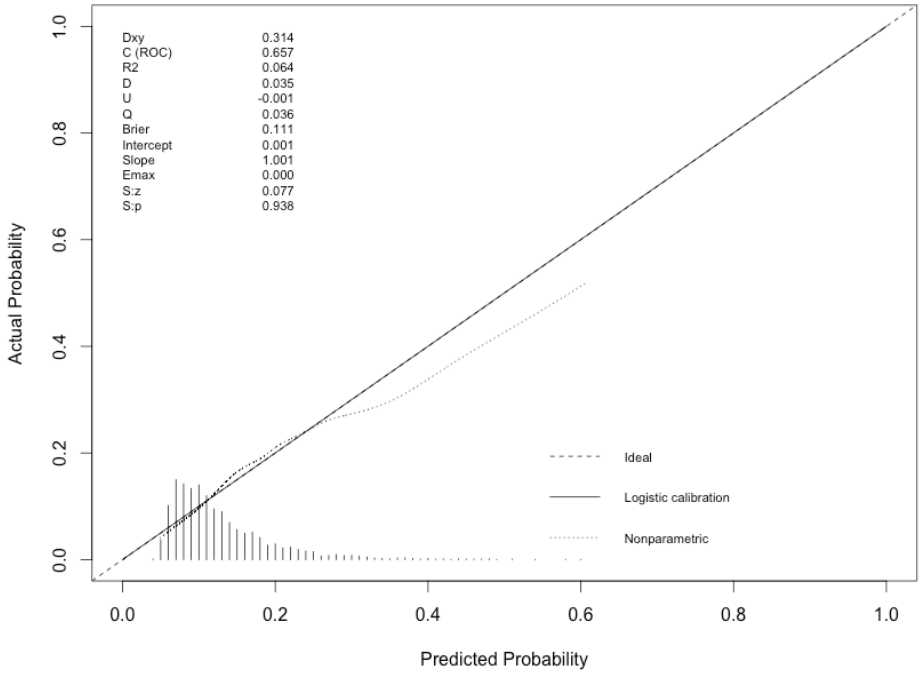


Figure 10: Model performance plot for outpatient group.

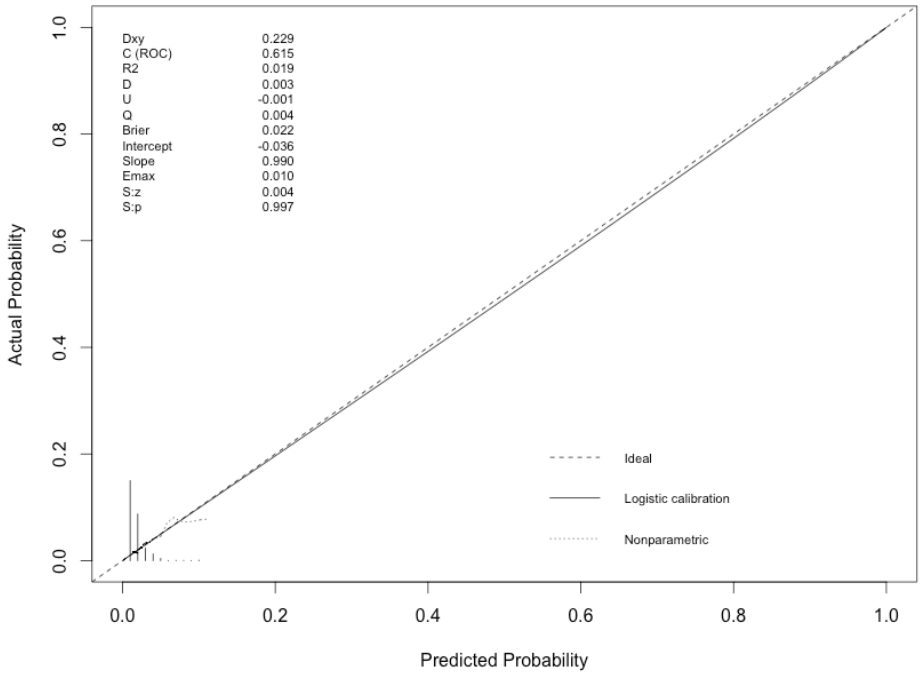


Figure 11: Model performance plot for anorectal group.

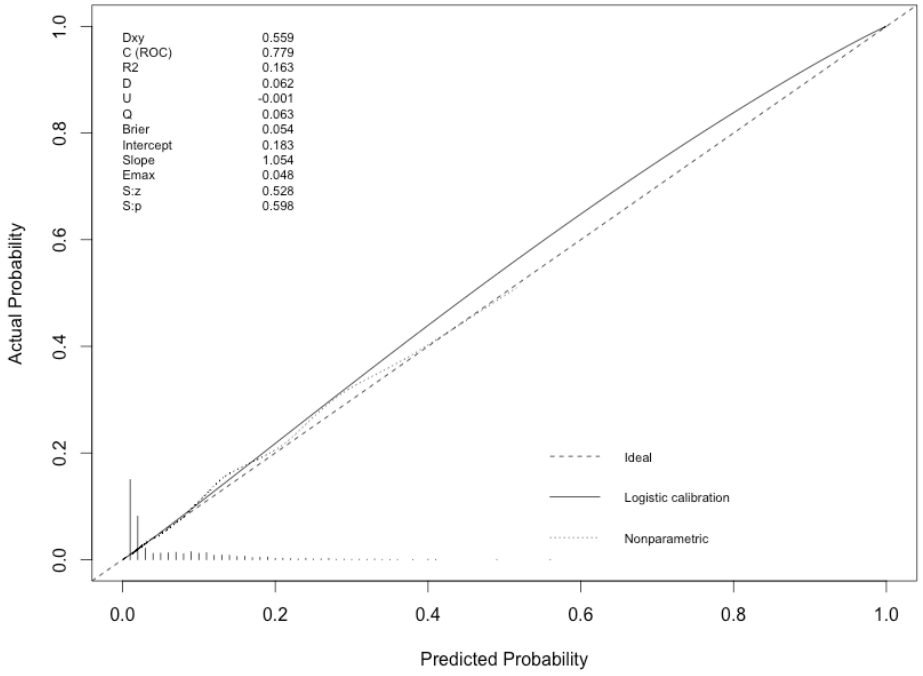


Figure 12: Model performance plot for abdominopelvic group.

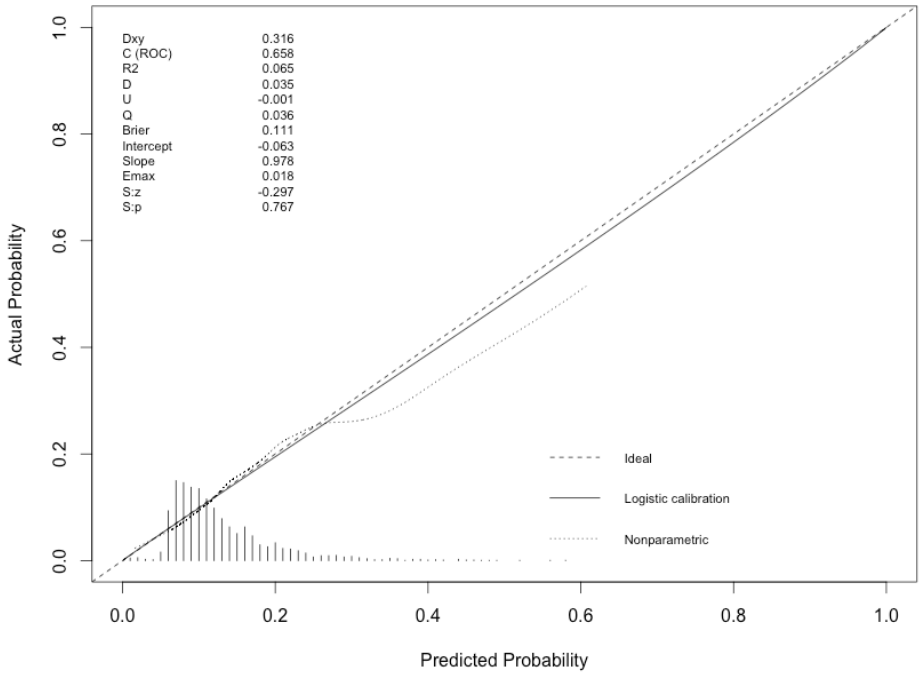


Figure 13: Model performance plot for elective surgery group.

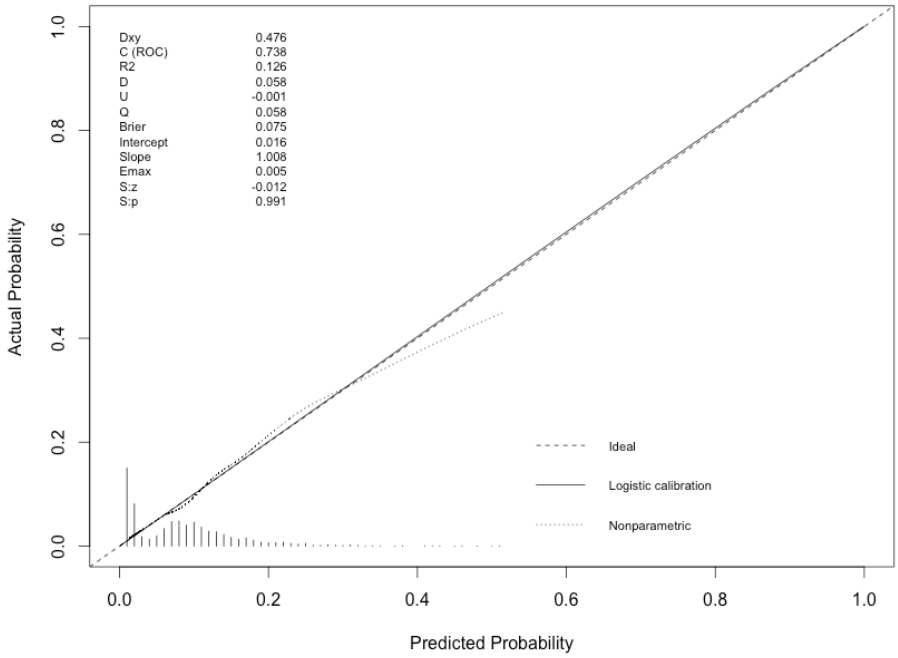
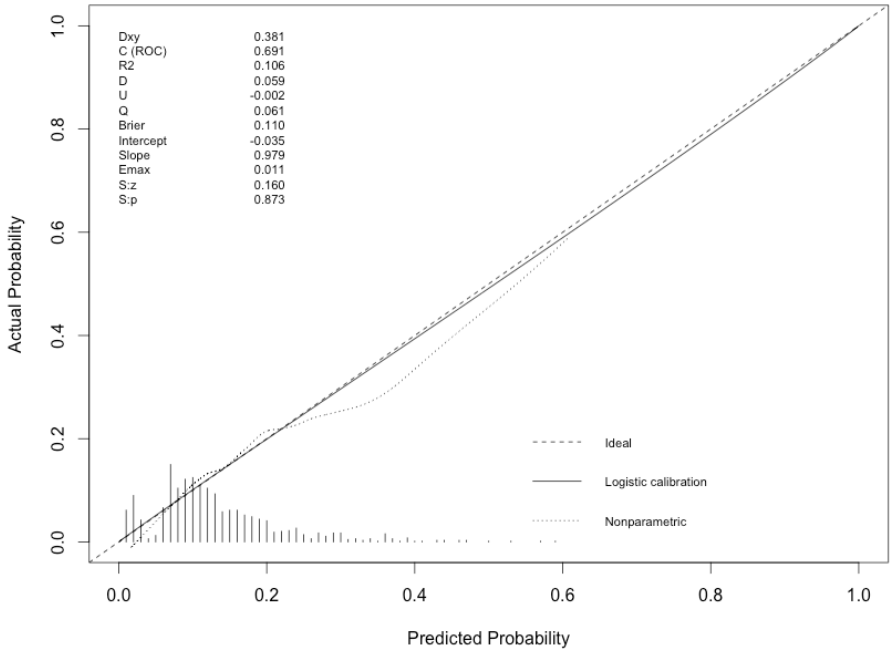


Figure 14: Model performance plot for urgent surgery group.



Model validation:

The final model was internally validated using a bootstrapping method. 2000 samples were replicated using this method. The c-statistic for the bootstrapped samples was 0.732. The bootstrapping produced a pseudo R square statistic of 0.128 and Brier score of 0.084.

DISCUSSION

We found that about one out of ten operative encounters result in hospital readmission within 30-days of discharge for patients who had colorectal surgery. Our results showed that length of stay, inpatient, comorbidity score, surgery time and anxiolytic use all had a statistical significant positive association with readmission risk after colorectal surgery (p-value < 0.05). Younger patient age and urgent surgery had a positive association with readmission risk, but were not statistically significant (p-value ≥ 0.05). Furthermore, we found that alcohol drinking had a statistically significant negative association with readmission risk (p-value < 0.05).

A model combining these risk factors can help policy makers and colorectal surgeons, specifically, better plan and care for their patients. It may also help researchers plan for future research by estimating readmission rates based on known patient characteristics. Our model uses simple clinical information that is easily available in the electronic medical record. It performs moderately well within the original data that was used to develop it and within the bootstrapped dataset.

Reported hospital readmission rates for mixed surgical population ranges between 5.7% and 12.3%.[3,4,18,31-34] In contrast, hospital readmission rates for colorectal surgery population are between 7.3% and 20%.[2-12] Our readmission rate was within the reported range described in the literature. A systemic review of risk prediction models for medical

hospital readmission showed that models vary in discrimination ability (c-statistic range: 0.55-0.83). [27] The review also found that predictive models with the best performance are, like our model, designed to possibly be used at hospital discharge (c-statistic range: 0.68-0.83). A study on readmission after mixed type of surgeries showed that a simple model that contains ASA score and length of stay during index admission had a c-statistics of 0.696 for readmission risk after surgery. [18] Our model performed fairly well compared to readmission model published in literature (c-statistics of 0.732).

Studies that investigated readmission differ in their methodology and approach. For instance, there is a variation in the readmission definition used among different studies. Some investigators examine readmissions that occur within 30-days, while others extend the definition to 90-days. [35] Moreover, differences exist about whether to use the discharge date or surgery date as the start date of readmission. The National Surgical Quality Improvement Program defines readmission as any admission within 30-days of index surgery. [36] On the other hand, CMS defines readmission as any admission to hospital within 30-days of a discharge from the same or another hospital. [15] We adapted the CMS definition because of the real world consequences of high readmission rates in reimbursement algorithms. Furthermore, more than 80% of unplanned readmissions after colorectal surgery happen within 30-days of hospital discharge. [37] Awareness about potential variation in research methodology in readmission studies is essential to accurately interpret results. It is very important that scientific investigators clearly elaborate on these aspects to better inform the scientific medical literature.[35]

We found that patients who use anxiolytics are more likely to be readmitted. While causal interpretations should be made cautiously, temporary discontinuation of anxiolytic medication for short periods prior or after surgery may contribute to readmission rates, as might an underlying proclivity to anxiety. Scientific evidence on the influence of anxiety on the increase risk of readmission for medical and surgical conditions does exist; [38,39] our results further underscore that psychological history is important for surgeons to consider.

Evidence-based interventions and programs that focus on educating and engaging patients in self-care, thereby facilitating care transitions, displayed a considerable reduction in readmissions. [40-43] Li et al. proposed a similar patient-centered early warning system, which is yet to be validated, to reduce readmission rates after colorectal surgery. [44] In trauma surgery, a proactive multidisciplinary team approach and involvement of nurse practitioners had some efficacy in lowering readmission risk for inpatient trauma cases. [45] Similar interventions to reduce readmission are needed in colorectal surgery that should include the risk factors outlined as important from our study. Our model can help to better plan and implement such interventions by identifying high risk patients to focus efforts on them.

Our study is limited by our inability to capture readmissions or deaths that happen outside of the study center. This could result in under estimation of the true readmission rate and may introduce bias to our model. We tried to compensate for this by reviewing electronic medical records for evidence of readmission to other hospitals. Additionally,

the generalizability of our finding is potentially limited by being a single center study. Although numerous studies have demonstrated a strong association between postoperative complications and hospital readmission, [3-6,8,9,11,12,31-34,46] we didn't evaluate the effect of postoperative complications on readmission risk. The database we used doesn't separate pre- and post-discharge complications and thus make it not an eligible variable to be used in predictive model intended to be used at discharge. Moreover, because of the retrospective nature of our study design, alcohol and tobacco use may have been underreported and misclassified. Finally, we couldn't examine the dose effect in alcohol because the amount of drinks is not reported in our database. It could be that the relation with readmission is the opposite for heavy drinkers compared to occasional drinkers.

While we were not able to externally validate our model, we used bootstrapping methods to internally validate our model. Our result showed very little evidence of overfitting or optimism on bootstrap validation, although we did not evaluate the effect of variable selection. Because of lack of external validation, we can't comment on how our model will perform in a different population of colorectal surgery patients.

In conclusion, certain clinical and demographic factors are associated with risk of hospital readmission after colorectal surgery. Furthermore, the risk of hospital readmission after a colorectal surgery can be predicted using a simple predictive model that includes age, length of stay, patient setting, comorbidity score, use of alcohol, surgery time, surgery urgency and use of anxiolytics medications. The model preforms

moderately well in discriminating patients who are high risk and low risk for readmission. The model is intended to be used before discharging patients from hospital after having a colorectal surgery. The model can help colorectal surgeons and hospitals in identifying high risk patient and focusing resources and efforts on them in attempt to reduce cost and improve quality of care. However, future studies are needed to externally validate this model and to test its impact on clinical care.

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